

## Adding Insult to Infection Pollution Exacerbates the Common Cold

Coming down with a cold caused by one of the many types of rhinoviruses is bad enough, but new research indicates that common pollutants can interact with respiratory cells to make the cold even worse than normal [*EHP* 110:665–670]. E. William Spannake, professor and associate chairman of the Department of Environmental Health Sciences at the Johns Hopkins Bloomberg School of Public Health, and colleagues were able to confirm that, when added to the insult of infection with rhinovirus, exposure to two common polluting gases results in a greater release of cytokines, inflammatory agents that are part of the molecular cascade that makes cold sufferers feel miserable.

“We have recognized for many years that environmental agents can modify the course of respiratory viral infections, and ambient levels of these agents have been proposed to play a role in modulating disease severity and health outcomes in exposed individuals,” the team wrote. For this study, Spannake and colleagues wanted to investigate the specific interactive effects of human rhinovirus type 16 and the oxidants nitrogen dioxide and ozone on markers of proinflammatory activity in human bronchial and nasal epithelial cells.

The team obtained nasal tissues removed from patients undergoing elective surgery to treat chronic rhinosinusitis. They isolated nasal epithelial cells from these normal tissues, some of which were then infected with rhinovirus and some not. Cells in both groups were then exposed to either normal air or air containing various concentrations of nitrogen dioxide or ozone.

The researchers observed that the double insult to the cells of both rhinovirus and one of the two pollutants resulted in an enhanced release of cytokines, particularly interleukin-8 and the surface expression of intercellular adhesion molecule 1. For example, the increases above the levels seen at single exposures were 41% higher when nitrogen dioxide was added to the mix at a dilution of 1:3,000. At a more concentrated 1:1,000 dilution, the release of the cytokines was 191% higher than predicted. At a 1:300 dilution, cytokine release increased 250%. When the team exposed rhinovirus-infected cells to ozone, the increases were less pronounced but still ranged between 41% and 67% above that expected from the responses to virus and ozone administered separately.

According to Spannake, this effect is additive, and in some cases more than additive—synergistic. Epithelial cells of both the upper and lower respiratory tract seem to be similarly affected, indicating a systemic effect. In addition to colds, virus-induced inflammation in the respiratory tract is also implicated in the exacerbation of asthma symptoms in some asthma patients.

However, Spannake says that further studies need to be designed and performed to determine if the laboratory findings can be correlated to clinical findings. “We do not presently know the extent to which indoor and outdoor oxidant pollutants may enhance these effects of rhinovirus in allergic asthmatics,” he says. —Ed Susman



**Nothing to sneeze at.** New research shows that pollution, particularly nitrogen dioxide, can exacerbate the inflammatory reactions in the respiratory system caused by the common cold.

## Processing Arsenic Genes Have a Say in How It's Metabolized

Arsenic has become notorious as a contaminant in drinking water worldwide because long-term ingestion of its inorganic form causes cancer and skin lesions. Studies are showing that some people are more affected by arsenic than others, probably due to genetic differences in how their bodies process the chemical. Now researchers from the University of California at Berkeley School of Public Health evaluate for the first time the degree to which family members resemble each other in their arsenic methylation capacities [*EHP* 110:729–733].

Joyce S. Chung and colleagues analyzed the urinary arsenic concentrations of 44 members of 11 Chilean families. The families all drank from one water source in their desert town of Chiu Chiu. The arsenic concentrations in the water were 750–800 µg/L, more than 70 times the new standard in the United States of 10 µg/L.

Arsenic is metabolized when enzymes in the body attach a methyl group to it. Inorganic arsenic is converted first to

monomethylarsenate and then to dimethylarsinate. The relative concentration of each in the urine is known as the methylation pattern.

The researchers compared methylation patterns among family members. Siblings had more similar patterns with each other than with their parents, and more similar patterns with their parents than with nonrelatives. For example, the correlations for one measurement of methylation were 0.72 between siblings and 0.18 for parents after adjusting for other factors that may affect methylation patterns, such as age, sex, micronutrient levels, and total urinary arsenic. Whether nutritional factors and gene–environment interactions affect methylation patterns remains unclear and requires further study, the team noted.

The fact that sibling and parent–child pairs had greater correlation than nonrelative pairs demonstrates that the variation in arsenic methylation probably has a genetic basis, something that researchers had expected but had not previously shown. Genetic polymorphisms have already explained differences in other methylation systems, such as those for metabolizing drugs.

Researchers once thought that methylation reduced the toxicity of arsenic. However, it is now believed that the methylated forms of arsenic may be more toxic than arsenic itself and may be more important in the development of cancer and skin lesions, the team wrote.

Understanding methylation patterns and whether arsenic poisoning is worse in certain families may eventually have clinical benefits. “If one person is identified with an arsenic-caused disease, other family members could be screened,” says coauthor Allan H. Smith. “In the long term, it might be possible to identify people who would be particularly susceptible and then minimize any exposure.” —**Tina Adler**

## A Causal Connection

### Cadmium Damages Kidneys and Bones

Long-term exposure to cadmium has long been suspected of causing kidney and bone damage in humans. Until now, the most common method of assessing the body burden of cadmium has been to measure the presence of cadmium in urine. However, elevated concentrations of cadmium in urine can also be caused by renal dysfunction, and this potentially confounding factor has left open to question any results that imply a direct causal link between cadmium exposure and adverse kidney and bone effects. In this month’s issue, researchers from the Karolinska Institute in Sweden led by Tobias Alfvén use measurements of cadmium in blood to strengthen the evidence that such a causal link does in fact exist [*EHP* 110:699–702].

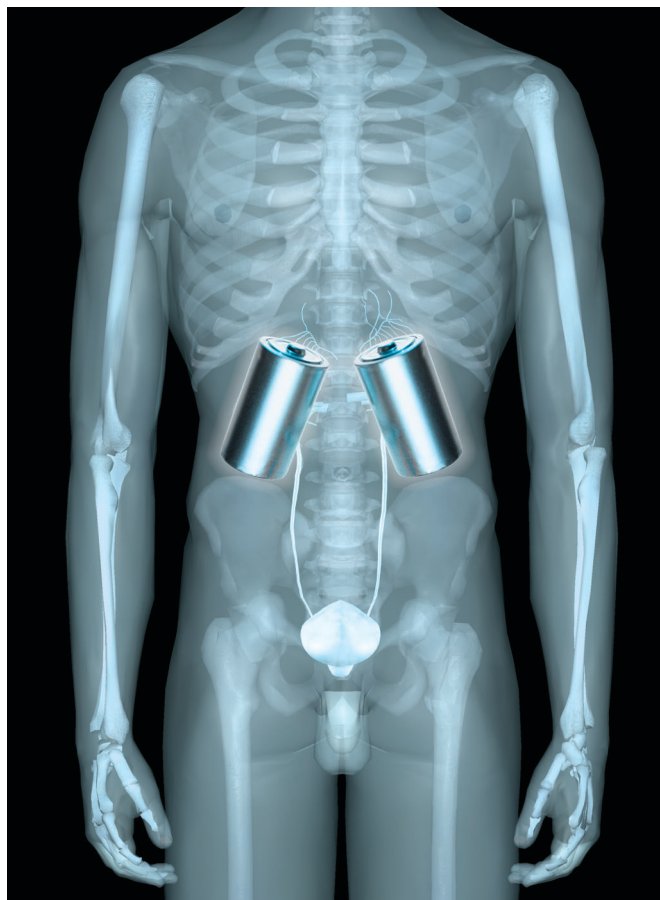
The investigators studied 1,021 residents of two communities in southeastern Sweden with documented cadmium and lead pollution. The pollution was a result of two local factories’ production of nickel–cadmium and lead batteries over the course of many decades. The subjects were required to have lived in the area for at least five years between 1910, when battery production began, and 1992. One hundred seventeen of the subjects currently or had previously worked in one of the battery plants and were considered occupationally exposed to the pollutants.

The authors measured blood lead and cadmium concentrations among the subjects, and also looked at the incidence of two conditions. The first, low bone mineral density, is a marker for osteoporosis. The second, tubular proteinuria (an increase in the presence of low-molecular-weight proteins in the urine), is an indication of kidney dysfunction.

The authors found no associations between lead and low bone mineral density or tubular proteinuria. In the case of cadmium, however, the researchers found a clear relationship between blood concentrations and both conditions. That relationship was particularly strong for tubular proteinuria.

Even when the occupationally exposed participants were excluded, the subgroup with the highest blood cadmium concentrations had a fourfold increased risk of having tubular proteinuria, compared with the subgroup with the lowest blood cadmium concentrations. It’s also interesting to note that even 15 years after the cessation of exposure, cadmium-exposed workers showed a stronger association between blood cadmium and tubular proteinuria than between urinary cadmium and tubular proteinuria, implying that there may be a dose–response relationship involved.

Like lead, cadmium apparently accumulates in the body, and even after exposure ceases, the concentration in the blood will not decrease to the preexposure level. The authors found that the effect of cadmium on bone mineral density was much more pronounced in older people. In the older group (more than 60 years old), the risk of low bone mineral density for the subgroup with the highest blood cadmium concentrations was almost three times that of the group with the lowest blood cadmium concentrations. Whether this is attributable to bone becoming more sensitive to cadmium as it ages or to the fact that it could take decades for cadmium to affect bone, or to both of these explanations, it’s still an alarming relationship. —**Ernie Hood**



**Assault and battery.** New research assessing blood cadmium concentrations in residents of communities near battery factories provides strong evidence of a link between exposure and damage to kidneys and bones.